Ms. Delora Dillard, OIPE

FROM: Anne-Marie Corrigan, STIC
           571-272-2501

Per your request, please find re-run of latest raw sequence listing (RSL) of 10/658355.
Total pages: 9, includes cover sheet.

Thank you.

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STIC Biotechnology Systems Branch

RAW SEQUENCE LISTING
ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information Center (STIC) detected errors when processing the following computer readable form:

Application Serial Number: _10/658,355A_

Source: _1F40_

Date Processed by STIC: _3/16/04_

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:
1) **INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE APPLICANT, WITH A NOTICE TO COMPLY or,**
2) **TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A NOTICE TO COMPLY**
FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE <u>CHECKER</u> <u>VERSION 4.2.2 PROGRAM</u>, ACCESSIBLE THROUGH THE U.S. PATENT AND TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:
      http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
<u>Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:</u>

1. EFS-Bio (<<u>http://www.uspto.gov/ebc/efs/downloads/documents.htm</u>> , EFS Submission User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 01/14/05):
   U.S. Patent and Trademark Office, Mail Stop Sequence, Customer Window, Randolph Building, 401 Dulany Street, Alexandria, VA 22314

Revised 01/24/05.

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Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: 10/658,355A

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1 ___ Wrapped Nucleics
Wrapped Aminos — The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."

2 ___ Invalid Line Length — The rules require that a line not exceed 72 characters in length. This includes white spaces.

3 ___ Misaligned Amino
Numbering — The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.

4 ___ Non-ASCII — The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.

5 ___ Variable Length — Sequence(s) ___ contain n's or Xaa's representing more than one residue. Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.

6 ___ PatentIn 2.0
"bug" — A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) ___. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.

7 ___ Skipped Sequences
(OLD RULES) — Sequence(s) ___ missing. If intentional, please insert the following lines for each skipped sequence:
(2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
(i) SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
This sequence is intentionally skipped

Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.

8 ___ Skipped Sequences
(NEW RULES) — Sequence(s) ___ missing. If intentional, please insert the following lines for each skipped sequence.
<210> sequence id number
<400> sequence id number
000

9 ___ Use of n's or Xaa's
(NEW RULES) — Use of n's and/or Xaa's have been detected in the Sequence Listing.
Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.

10 ___ Invalid <213>
Response — Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence

11 ___ Use of <220> — Sequence(s) ___ missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.
(See "Federal Register," 00/01/1998, Vol. 63, No. 104, pp. 29631-32) (See 1.823 of Sequence Rules)

12 ___ PatentIn 2.0
"bug" — Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

13 ___ Misuse of n/Xaa — "n" can only represent a single nucleotide; "Xaa" can only represent a single amino acid

AMC – Biotechnology Systems Branch – 09/09/2003

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IFWO

RAW SEQUENCE LISTING   DATE: 03/16/2004
PATENT APPLICATION: US/10/658,355A   TIME: 07:58:57

Input Set : D:\923seq.002
Output Set: N:\CRF4\03162004\J658355A.raw

```
 3 <110> APPLICANT: Gantier, Rene
 4         Guyon, Thierry
 5         Hugo, Cruz Ramos
 6         Vega, Manuel
 7         Drittanti, Lila
 9 <120> TITLE OF INVENTION: Rational Directed Protein Evolution Using Two Dimensional
10         Rational
11         Mutagenesis Scanning
13 <130> FILE REFERENCE: 38751-923
15 <140> CURRENT APPLICATION NUMBER: US/10/658,355A
16 <141> CURRENT FILING DATE: 2003-09-08
18 <150> PRIOR APPLICATION NUMBER: 60/457,063
19 <151> PRIOR FILING DATE: 2003-03-21
21 <150> PRIOR APPLICATION NUMBER: 60/410,258
22 <151> PRIOR FILING DATE: 2002-09-09
24 <160> NUMBER OF SEQ ID NOS: 501
25 <170> SOFTWARE: FastSEQ for Windows Version 4.0
```

Does Not Comply
Corrected Diskette Needed

(pg. 1 — 6)

ERRORED SEQUENCES

```
      7445 <210> SEQ ID NO: 182
      7446 <211> LENGTH: 55
      7447 <212> TYPE: DNA
      7448 <213> ORGANISM: Artificial Sequence
      7450 <220> FEATURE:
      7451 <223> OTHER INFORMATION: EcoRI Forward Primer
      7453 <400> SEQUENCE: 182
E--> 7454 gcctgtatga tttattggat gttggaattc cctgatgcgg tattttctcc ttacg
   -  7455 (55)
      7457 <210> SEQ ID NO: 183
      7458 <211> LENGTH: 55
      7459 <212> TYPE: DNA
      7460 <213> ORGANISM: Artificial Sequence
      7462 <220> FEATURE:
      7463 <223> OTHER INFORMATION: EcoRI Reverse Primer
      7465 <400> SEQUENCE: 183
E--> 7466 cgtaaggaga aaataccgca tcagggaatt ccaacatcca ataaatcata caggc
      7467 (55)
      7469 <210> SEQ ID NO: 184
      7470 <211> LENGTH: 35
      7471 <212> TYPE: DNA
      7472 <213> ORGANISM: Artificial Sequence
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[handwritten annotations: "please see item # 1 on error summary sheet.", "55 insert here", "55 insert here"]

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PAGE 4/9 * RCVD AT 5/9/2005 9:35:48 AM [Eastern Daylight Time] * SVR:USPTO-EFXRF-2/3 * DNIS:7466621 * CSID:703 308 4221 * DURATION (mm-ss):03-28

same errors

```
7474 <220> FEATURE:
7475 <223> OTHER INFORMATION: Seq ClaI Forward Primer
7477 <400> SEQUENCE: 184
E--> 7478 ctgcttatca accgcggtac atatgattga catgc
7479 (35)
7481 <210> SEQ ID NO: 185
7482 <211> LENGTH: 31
7483 <212> TYPE: DNA
7484 <213> ORGANISM: Artificial Sequence
7486 <220> FEATURE:
7487 <223> OTHER INFORMATION: Seq ClaI Reverse Primer
7489 <400> SEQUENCE: 185
E--> 7490 tacgggataa taccgcgcca catagcagaa c
7491 (31)
7493 <210> SEQ ID NO: 186
7494 <211> LENGTH: 18
7495 <212> TYPE: DNA
7496 <213> ORGANISM: Artificial Sequence
7498 <220> FEATURE:
7499 <223> OTHER INFORMATION: Seq Forward Primer
7501 <400> SEQUENCE: 186
E--> 7502 cctgatgaag gaggactc
7503 (18)
7505 <210> SEQ ID NO: 187
7506 <211> LENGTH: 18
7507 <212> TYPE: DNA
7508 <213> ORGANISM: Artificial Sequence
7510 <220> FEATURE:
7511 <223> OTHER INFORMATION: Seq Reverse Primer
7513 <400> SEQUENCE: 187
E--> 7514 ccaagcagca gatgagtc
7515 (18)
7517 <210> SEQ ID NO: 188
7518 <211> LENGTH: 31
7519 <212> TYPE: DNA
7520 <213> ORGANISM: Artificial Sequence
7522 <220> FEATURE:
7523 <223> OTHER INFORMATION: IFN alpha-2b 5' Primer
7525 <400> SEQUENCE: 188
E--> 7526 tcagctgcaa gtcaagctgc tctgtgggct g
7527 (31)
7529 <210> SEQ ID NO: 189
7530 <211> LENGTH: 48
7531 <212> TYPE: DNA
7532 <213> ORGANISM: Artificial Sequence
7534 <220> FEATURE:
7535 <223> OTHER INFORMATION: IFN alpha-2b 3' Primer
7537 <400> SEQUENCE: 189
E--> 7538 gctctagatc attccttact tcttaaactt tcttgcaagt ttgttgac
```

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PAGE 5/9 * RCVD AT 5/9/2005 9:35:48 AM [Eastern Daylight Time] * SVR:USPTO-EFXRF-2/3 * DNIS:7466621 * CSID:703 308 4221 * DURATION (mm-ss):03-28

RAW SEQUENCE LISTING   DATE: 03/16/2004
PATENT APPLICATION: US/10/658,355A   TIME: 07:58:58

Input Set : D:\923seq.002
Output Set: N:\CRF4\03162004\J658355A.raw

same errors

```
        7539   48
        7541  <210> SEQ ID NO: 190
        7542  <211> LENGTH: 36
        7543  <212> TYPE: DNA
        7544  <213> ORGANISM: Artificial Sequence
        7546  <220> FEATURE:
        7547  <223> OTHER INFORMATION: IFN alpha-2b HindIII Primer
        7549  <400> SEQUENCE: 190
E--> 7550  ccgaagctta tggccttgac ctttgcttta ctggtg          36
        7551  (36)
        7553  <210> SEQ ID NO: 191
        7554  <211> LENGTH: 48
        7555  <212> TYPE: DNA
        7556  <213> ORGANISM: Artificial Sequence
        7558  <220> FEATURE:
        7559  <223> OTHER INFORMATION: IFN alpha-2b XbaI Primer
        7561  <400> SEQUENCE: 191
E--> 7562  gctctagatc attccttact tcttaaactt tcttgcaagt ttgttgac   48
        7563  (48)
        7565  <210> SEQ ID NO: 192
        7566  <211> LENGTH: 80
        7567  <212> TYPE: DNA
        7568  <213> ORGANISM: Artificial Sequence
        7570  <220> FEATURE:
        7571  <223> OTHER INFORMATION: IFN alpha-2b 80 bp 5' Primer
        7573  <400> SEQUENCE: 192
E--> 7574  cccaagctta tggccttgac ctttgcttta ctggtggccc tcctggtgct cagctgcaag  60
E--> 7575 (80)
E--> 7576  tcaagctgct ctgtgggctg                                80
        7578  <210> SEQ ID NO: 193
        7579  <211> LENGTH: 20
        7580  <212> TYPE: DNA
        7581  <213> ORGANISM: Artificial Sequence
        7583  <220> FEATURE:
        7584  <223> OTHER INFORMATION: EMCV Forward Primer
        7586  <400> SEQUENCE: 193
E--> 7587  ccgctacatt gaggcatcca
        7588  (20)
        7590  <210> SEQ ID NO: 194
        7591  <211> LENGTH: 21
        7592  <212> TYPE: DNA
        7593  <213> ORGANISM: Artificial Sequence
        7595  <220> FEATURE:
        7596  <223> OTHER INFORMATION: EMCV Reverse Primer
        7598  <400> SEQUENCE: 194
E--> 7599  caggagcagg acaaggtcac t
        7600  (21)
        7602  <210> SEQ ID NO: 195
        7603  <211> LENGTH: 22
```

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PAGE 6/9 * RCVD AT 5/9/2005 9:35:48 AM [Eastern Daylight Time] * SVR:USPTO-EFXRF-2/3 * DNIS:7466621 * CSID:703 308 4221 * DURATION (mm-ss):03-28

RAW SEQUENCE LISTING   DATE: 03/16/2004
PATENT APPLICATION: US/10/658,355A   TIME: 07:58:58

Same errors

Input Set : D:\923seq.002
Output Set: N:\CRF4\03162004\J658355A.raw

```
  7604 <212> TYPE: DNA
  7605 <213> ORGANISM: Artificial Sequence
  7607 <220> FEATURE:
  7608 <221> NAME/KEY: misc_feature
  7609 <222> LOCATION: 1; 22
  7610 <223> OTHER INFORMATION: EMCV Probe: n at position 1 is a 5-carboxyfluorescein
  7611       (FAM)-modified deoxycytidylate; n at position 22 is an N,N,N',N'-
  7612       tetramethyl-6-carboxyrhodamine (TAMRA)-modified deoxythymidylate.
  7614 <400> SEQUENCE: 195
E--> 7615 nagccgtca agacccaacc gcn
  7616      (22)
  8074 <210> SEQ ID NO: 208
  8075 <211> LENGTH: 41
  8076 <212> TYPE: DNA
  8077 <213> ORGANISM: Artificial Sequence
  8079 <220> FEATURE:
  8080 <223> OTHER INFORMATION: Oligonucleotide
  8082 <400> SEQUENCE: 208
E--> 8083 aacatatgtg tgatctgcct caaacccaca gcctgggtag c
  8084      (41)
  8086 <210> SEQ ID NO: 209
  8087 <211> LENGTH: 46
  8088 <212> TYPE: DNA
  8089 <213> ORGANISM: Artificial Sequence
  8091 <220> FEATURE:
  8092 <223> OTHER INFORMATION: Oligonucleotide
  8094 <400> SEQUENCE: 209
E--> 8095 aaggatcctc attccttact tcttaaactt tcttgcaagt ttgttg
  8096      (46)
  8098 <210> SEQ ID NO: 210
  8099 <211> LENGTH: 41
  8100 <212> TYPE: DNA
  8101 <213> ORGANISM: Artificial Sequence
  8103 <220> FEATURE:
  8104 <223> OTHER INFORMATION: Oligonucleotide
  8106 <400> SEQUENCE: 210
E--> 8107 aacatatgtg tgatctgcct caaacccaca gcctgggtag c
  8108      (41)
  8110 <210> SEQ ID NO: 211
  8111 <211> LENGTH: 46
  8112 <212> TYPE: DNA
  8113 <213> ORGANISM: Artificial Sequence
  8115 <220> FEATURE:
  8116 <223> OTHER INFORMATION: Oligonucleotide
  8118 <400> SEQUENCE: 211
E--> 8119 aaggatcctc attccttact tcttaaactt tcttgcaagt ttgttg
  8120      (46)
 19072 <210> SEQ ID NO: 500
 19073 <211> LENGTH: 46
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PAGE 7/9 * RCVD AT 5/9/2005 9:35:48 AM [Eastern Daylight Time] * SVR:USPTO-EFXRF-2/3 * DNIS:7466621 * CSID:703 308 4221 * DURATION (mm-ss):03-28

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                    RAW SEQUENCE LISTING                    DATE: 03/16/2004
                    PATENT APPLICATION:  US/10/658,355A     TIME: 07:58:59

                    Input Set : D:\923seq.002
                    Output Set: N:\CRF4\03162004\J658355A.raw
```

Same errors

```
     19074  <212> TYPE: DNA
     19075  <213> ORGANISM: Artificial Sequence
     19077  <220> FEATURE:
     19078  <223> OTHER INFORMATION: primer reverse INFA-E159H
     19080  <400> SEQUENCE: 500
E--> 19081  aaggatcctc attccttact tcttaaactg tgttgcaagt ttgttg
     19082  46
     19084  <210> SEQ ID NO: 501
     19085  <211> LENGTH: 46
     19086  <212> TYPE: DNA
     19087  <213> ORGANISM: Artificial Sequence
     19089  <220> FEATURE:
     19090  <223> OTHER INFORMATION: primer reverse INFA-E159Q
     19092  <400> SEQUENCE: 501
E--> 19093  aaggatcctc attccttact tcttaaactc tgttgcaagt ttgttg
     19094  46
```

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PAGE 8/9 * RCVD AT 5/9/2005 9:35:48 AM [Eastern Daylight Time] * SVR:USPTO-EFXRF-2/3 * DNIS:7466621 * CSID:703 308 4221 * DURATION (mm-ss):03-28

VERIFICATION SUMMARY　　　　　　　DATE: 03/16/2004
PATENT APPLICATION:　US/10/658,355A　　TIME: 07:59:00

Input Set : D:\923seq.002
Output Set: N:\CRF4\03162004\J658355A.raw

```
L:7454 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:55 SEQ:182
L:7466 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:55 SEQ:183
L:7478 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:35 SEQ:184
L:7490 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:31 SEQ:185
L:7502 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:18 SEQ:186
L:7514 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:18 SEQ:187
L:7526 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:31 SEQ:188
L:7538 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:48 SEQ:189
L:7550 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:36 SEQ:190
L:7562 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:48 SEQ:191
L:7574 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:60 SEQ:192
M:254 Repeated in SeqNo=192
L:7587 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:20 SEQ:193
L:7599 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:21 SEQ:194
L:7615 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:195 after pos.:0
L:7615 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:22 SEQ:195
L:8083 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:41 SEQ:208
L:8095 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:46 SEQ:209
L:8107 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:41 SEQ:210
L:8119 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:46 SEQ:211
L:19081 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:46 SEQ:500
L:19093 M:254 E: No. of Bases conflict, LENGTH:Input:0 Counted:46 SEQ:501
```

file://C:\CRF4\Outhold\VsrJ658355A.htm　　　　　　　　　　　　3/16/04

PAGE 9/9 * RCVD AT 5/9/2005 9:35:48 AM [Eastern Daylight Time] * SVR:USPTO-EFXRF-2/3 * DNIS:7466621 * CSID:703 308 4221 * DURATION (mm-ss):03-28